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B8N

Selected US specifications from IPC sub-classes

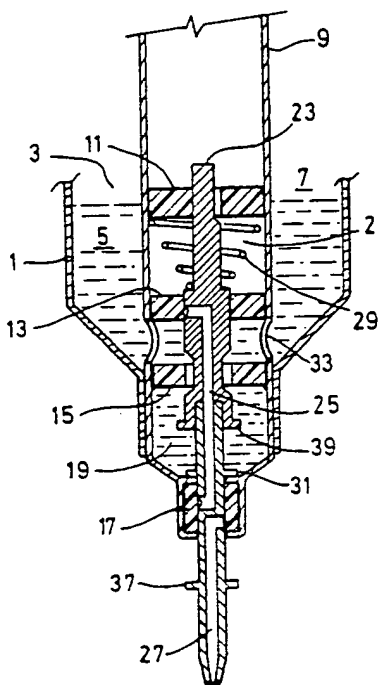
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(54) Pressurised metering dispenser; manual actuator; sampling

(57) A pressurised metering dispenser comprises a main reservoir (3), a liquid metering chamber (19) and a gas chamber (7). Valve means isolate the reservoir and the gas chamber from an outlet nozzle (27) at the end of a central passage (9), the inboard end of which is above the level of liquid in the reservoir (7) when the dispenser is held nozzle-down. A gas holding chamber (21) communicates with the gas chamber (7) and the liquid metering chamber (19) with the reservoir (3) in a normal state, and actuation is achieved by upward displacement of the nozzle (27) and valve member (23) to isolate liquid and gas holding chambers (21) and (19) from their supplies and finally cause the chamber (21) to communicate with the chamber (19) via passage (25) to cause the liquid to be expelled through the nozzle under gas pressure.

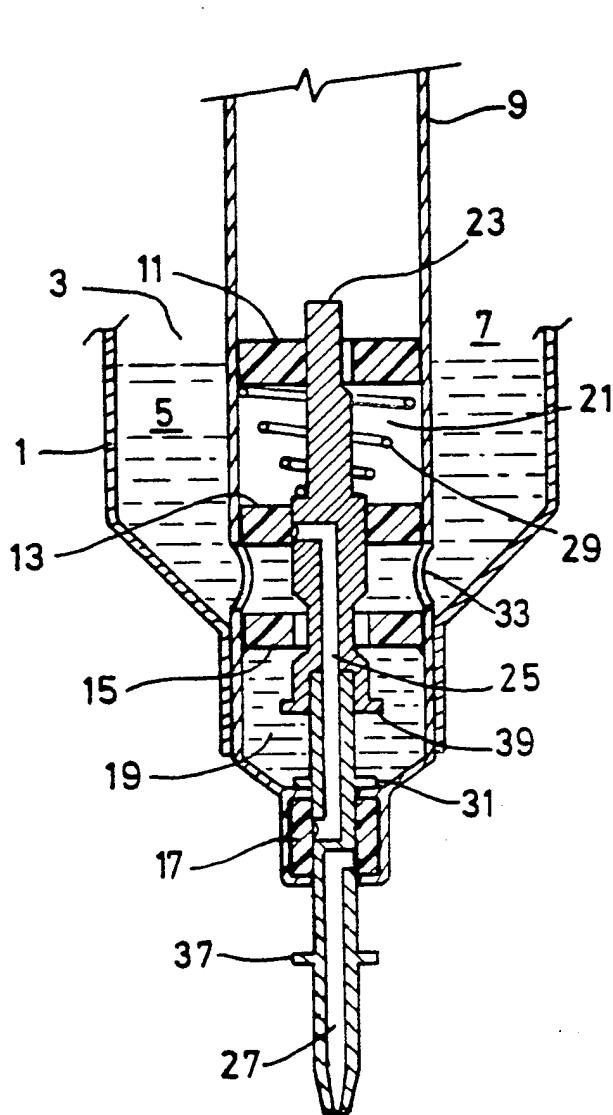
A holder for such a dispenser includes a manual actuating lever and counter to indicate the number of actuations.

A modified sampling dispenser includes a sleeve which is resiliently displaceable relative to the lower end of a nozzle and indicates an extension of known internal volume into which liquid can be drawn by upward displacement, for mixing with reagent subsequently ejected through the nozzle on actuation of the dispenser.



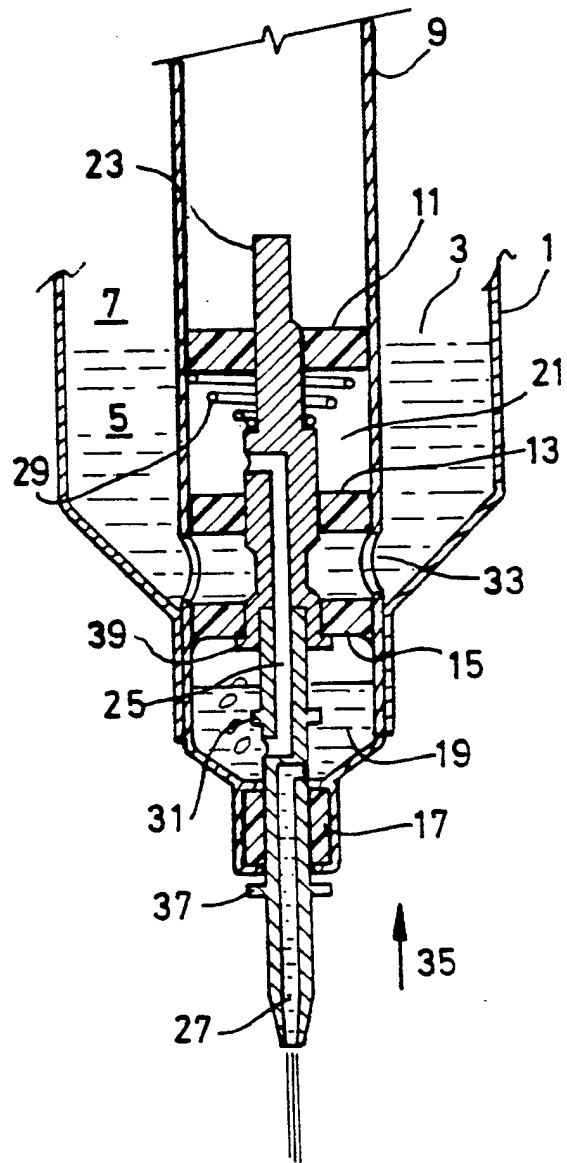
REFILL

Fig.1



REFILL

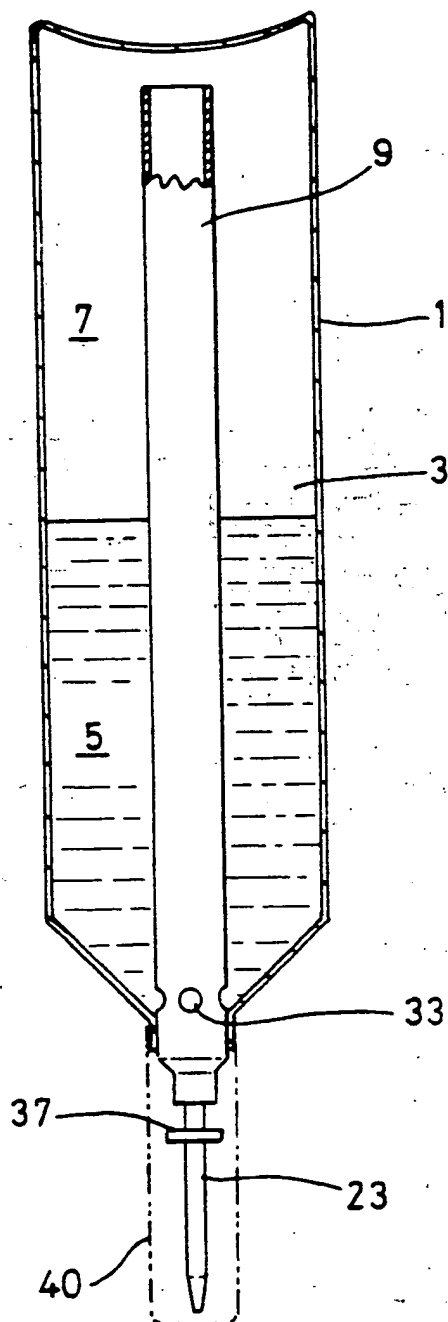
Fig. 1



DISCHARGE

Fig. 2

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*Fig. 3*

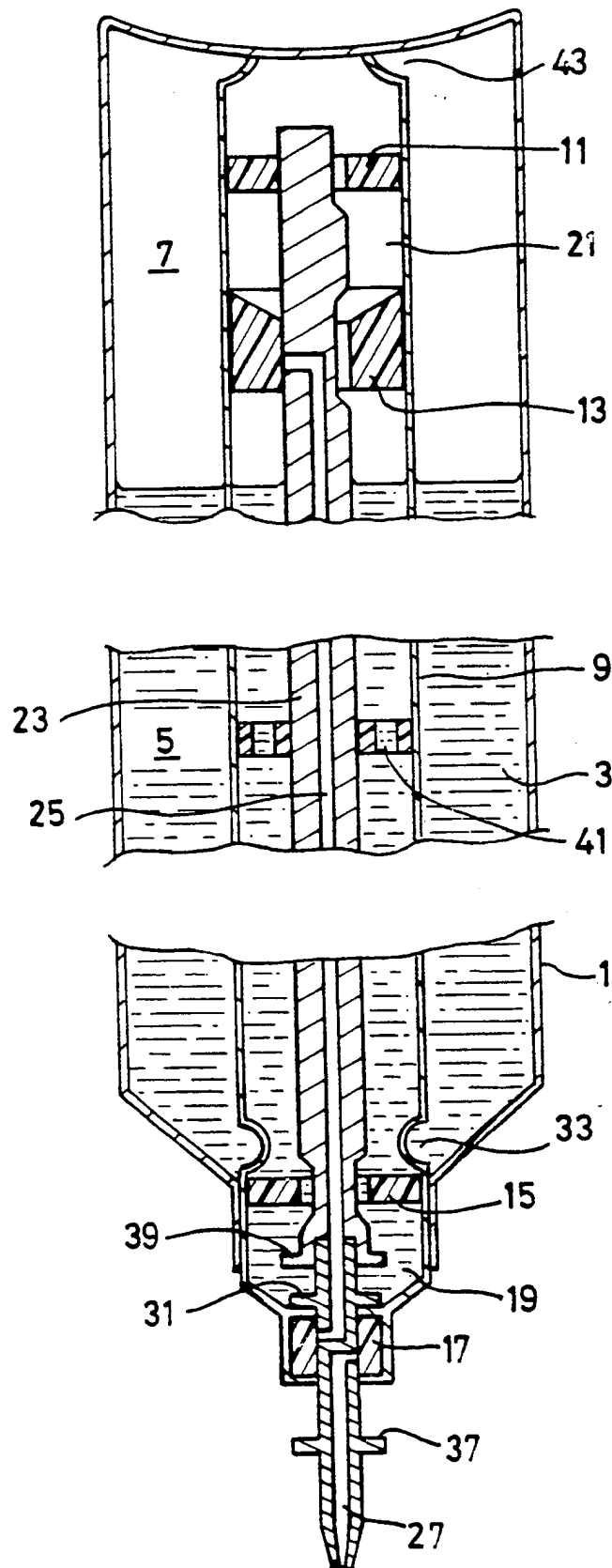
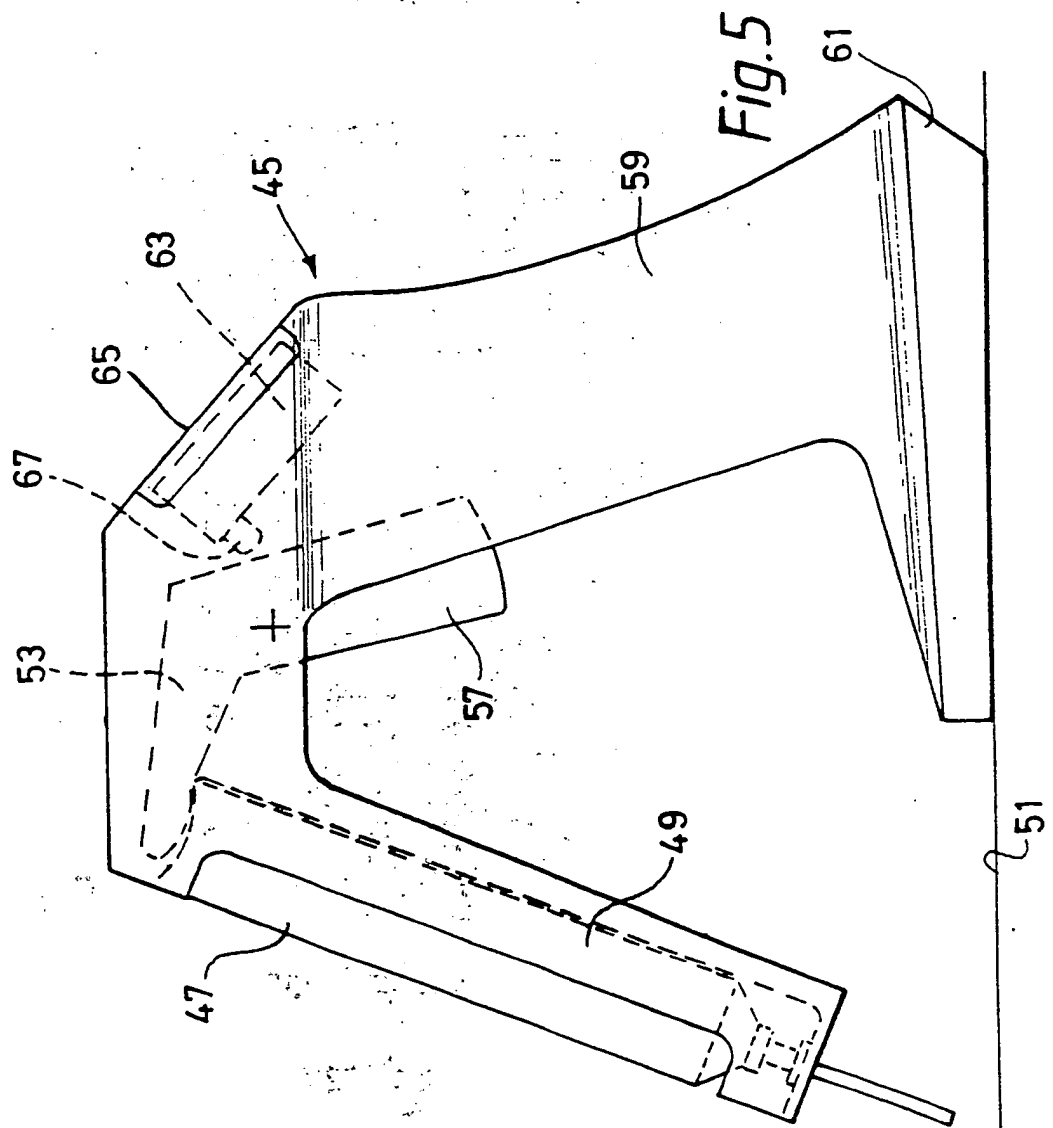
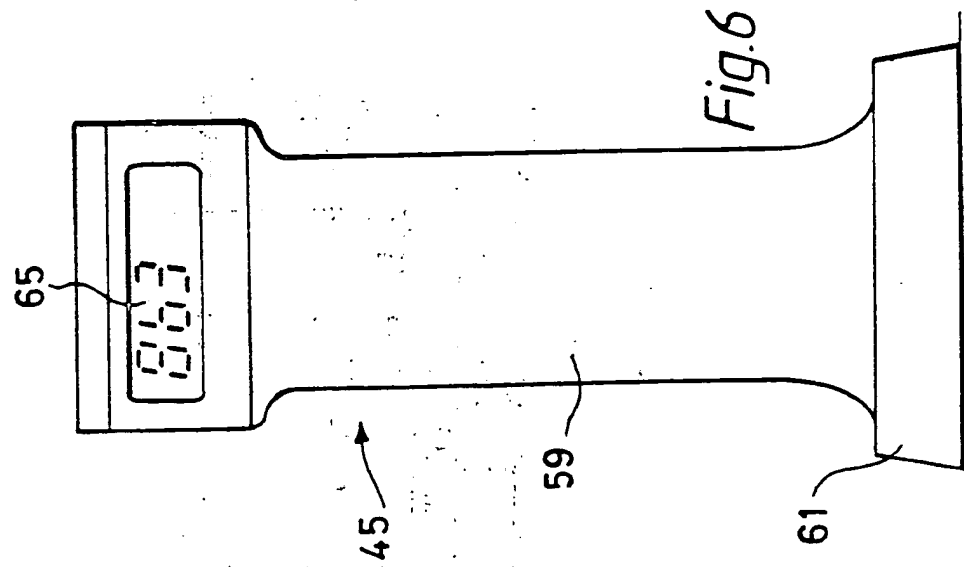
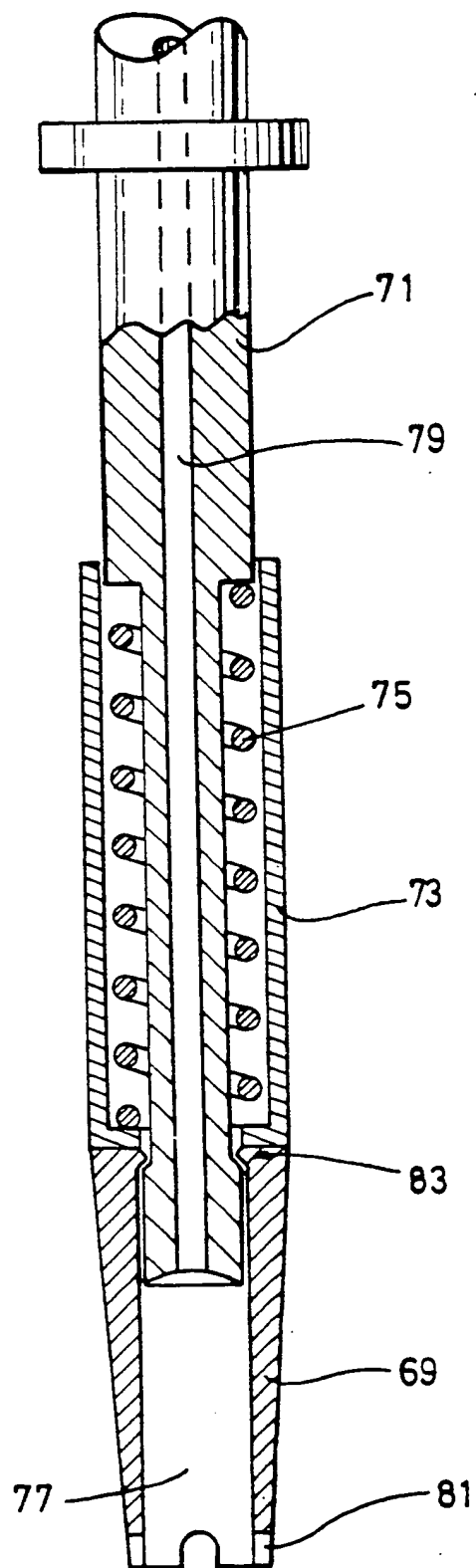


Fig.4

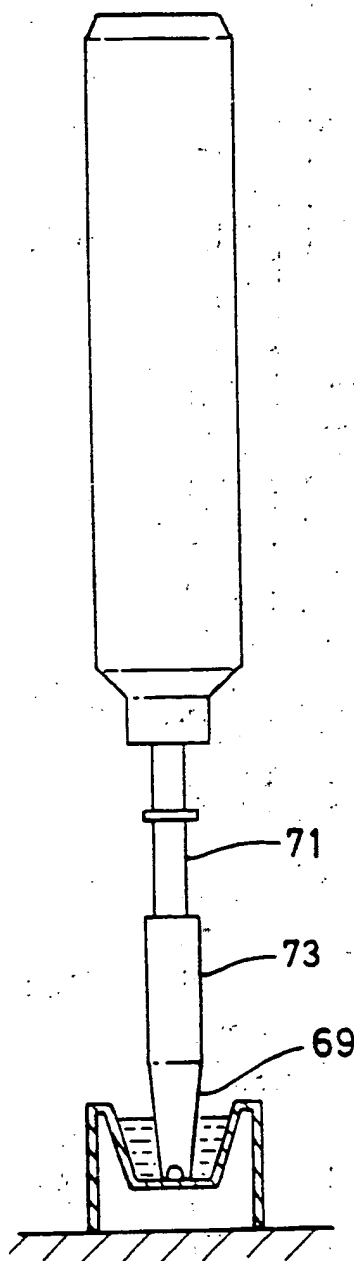
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*Fig 7*

6/6

*Fig. 8*

Description

Title: Pressurised Metering Dispenser

Field of the invention

5 The present invention relates to a pressurised metering dispenser and to a holder and actuator for pressurised metering dispensers.

Background of the invention

10 Metering liquid dispensers using gas pressure for discharging the liquid were invented in the 1950's. As with most common pressurised liquid dispensers, the liquid in such known metering dispensers is subdivided into minute droplets on leaving the dispenser, forming an aerosol.

15 The main use for such dispensers hitherto has been for administering metered doses of drugs for inhalation. Early forms of dispensers gave somewhat erratic metering, but improvements in valve designs and in formulations for the dispenser contents have led to pressurised metering liquid dispensers currently available which are capable of
20 ± 1% on the nominal metered volume dispensed.

However, further variations occur during the period of use of a dispenser, reducing the overall dispensing accuracy

to no better than $\pm 5\%$. One cause for this problem is that as the dispenser is used high vapour pressure components in the dispenser contents are preferentially discharged, and therefore depleted. Thus, when the dispenser is nearly empty the doses dispensed will have an increased concentration of low vapour pressure components, and the concentration of the active pharmaceutical ingredient may vary during the course of use of the dispenser.

A typical formulation in a known pressurised metering liquid dispensers used to administer pharmaceuticals for inhalation contains the pharmaceutical active ingredient, a mixture of propellents (typically fluorocarbons 11, 12 and 114), a low volatility excipient and valve lubricant such as sorbitan trioleate and anti-oxidants, in solution in ethanol.

The dispensers perform their metering function by means of a metering chamber located within the dispenser and normally open to the main dispenser reservoir containing the formulation. When the dispenser is held in the correct position for use, the metering chamber is lowermost and filled with formulation. During actuation of the dispenser, the metering chamber is first closed from the main reservoir and then connected to a discharge passage. The pressure of the propellents contained in the formulation will then drive the contents of the metering chamber out through the discharge passage. As the formulation is released into the atmosphere, any propellents still in liquid form will tend to vaporise, assisting in the formation of the aerosol, and the ethanol solvent will also tend to evaporate. This evaporation tends to chill the discharge nozzle of the dispenser, and

rapidly repeated discharges from the dispenser may result in the nozzle freezing.

5 In my co-pending applications 8608571 and 8624064, it is suggested that a pressurised 1-shot metering dispenser may be used to deliver reagents during chemical analysis. It has also now been realised that there are many other situations in which it would be convenient to be able to deliver precisely metered volumes of liquid from a pressurised dispenser. For example, in many circumstances
10 in medicine and chemistry it is necessary to prepare a sample before it can be analysed or studied. In such sample preparation, the sample may be diluted with distilled water or some other chemically pure diluant and stabilisers such as anti-oxidants, pH buffers etc may also
15 be added. All of these must be added in precisely known quantities if accurate results are to be obtained from subsequent study or analysis.

Typically, the dispensing of accurate volumes in such circumstances is at present carried out using various
20 types of pipettes and syringes. There are three main types of device in use. The first are "air pipettes", in which a squeeze-bulb or syringe sucks up liquid by reducing the air pressure in the pipette, and then small amounts of liquid are dispensed by mechanically indexing a
25 plunger. The second are positive displacement syringes, in which a plunger is brought up to the tip of the discharge nozzle and the syringe is filled and emptied by movement of the plunger. The third are single shot dispensers, which employ a pair of non-return valves and a
30 syringe which is alternately filled and emptied to discharge a fixed volume.

The first type is the least accurate because there is a volume of air between the reagent and the piston or plunger. The second type is the most accurate because it relies on the movement of a piston in a very accurate bore and there is no air cushion between the liquid and the piston. The third type is less precise but is suitable for dispensing liquids from a bulk container. The best figure for repeatability of the volume dispensed from one discharge to another of the same device is around $\pm 1\%$ for these types of device.

In addition to their lack of convenience, these devices suffer the following problems. First, the reagent or other liquid has to be drawn from a bulk supply, or made up immediately prior to use if it has a limited shelf life, and in all pipetting methods the liquid is in contact with the air during the dispensing operation. This provides opportunities for the liquid being dispensed to become contaminated by dust, dirt and bacteria, and the liquid itself may undergo a change through evaporation, oxidation or the like. Second, occasionally a droplet of liquid remains on the tip of the discharge nozzle of the device, so that one measure is under-volume and the next measure is over-volume. The range of metered volumes dispensed from such apparatus is typically from about 5 microlitres to 10 millilitres, and a droplet can represent a large percentage error at the lower end of this range.

In my earlier U.K. Patent application 8608571 and 8624064, it is proposed that reagents for chemical analysis could be pre-packaged in a pressurised metering dispenser, in which case contamination and errors due to droplets remaining on the discharge nozzle are much less likely to occur. Additionally, the reagents can be made up by the

5 manufacturer under controlled conditions to ensure
consistent high quality and can be used in an environment
in which the preparation of a reagent or its extraction
from a bulk supply are impractical. The same principle
can be used, and the same advantages obtained, in other
circumstances in which a precisely metered volume of
liquid is required to be dispensed.

10 However, the variation in the composition of the contents
of the dispenser during use, as referred to above, means
that the conventional arrangements for pressurised
metering liquid dispensers cannot normally be applied to
chemical analysis sample preparation etc. Additionally,
it is frequently a disadvantage when dispensing a metered
volume of liquid for the liquid to be dispensed in the
15 form of an aerosol, whereas with the conventional
pressurised dispenser arrangement the formation of an
aerosol as the liquid is discharged is usually
unavoidable. Furthermore, it is sometimes desired to
dispense a metered volume of the same liquid into each of
20 a series of containers in quick succession, in which case
the tendency of the nozzle of a conventional dispenser to
freeze on rapid repetition of discharges is inconvenient.

25 These difficulties with known pressurised metering
dispensers could be largely reduced if not overcome
completely by replacing the conventional fluorocarbon
propellant with a pressurised chemically inert gas
propellant such as nitrogen or argon, as is proposed in my
earlier applications. In the prior art dispensers, the
variation of the composition of the dispenser contents
30 with use is largely due to high vapour pressure components
in the propellant mix evaporating preferentially. If a
compressed gas propellant is used in place of a condensed

high vapour pressure substance the propellant does not dilute the liquid composition in the dispenser and thus the pattern of loss of propellant will have no effect on the concentration or composition of the liquid being
5 dispensed. Since the propellant is already gaseous and tends not to be mixed with the liquid during discharge, the formation of an aerosol can normally be avoided if this is desired (although if required an aerosol can be formed by appropriate shaping of the discharge nozzle).
10 Additionally, since the propellant is already gaseous it does not vapourise at the discharge nozzle so that the cooling of the discharge nozzle is greatly reduced.

Unfortunately, if such a gaseous propellant is used in place of the conventional fluorocarbon propellents in a
15 conventional pressurised metering dispenser, the dispenser is unlikely to function correctly. In order for the metering to be accurate, the metering chamber must be sealed from the main reservoir for the dispenser contents before the outlet valve is opened. However, this means
20 that the metering chamber is also sealed from the pressure prevailing in the main reservoir. Thus, if the liquid contained in the metering chamber does not include liquified admixed propellant, there will be no pressure within the metering chamber to drive the metered liquid
25 dose out of the dispenser when the outlet valve is opened.

Summary of the invention

According to the present invention there is provided a pressurised metering dispenser comprising a main
30 reservoir, a liquid metering chamber and a gas holding chamber, arranged so that if the main reservoir is charged

with a liquid and a pressurising gas and the dispenser is held in its position of use, the liquid metering chamber will normally be sealed from the environment and be in communication with the main reservoir to receive liquid therefrom and the gas holding chamber will normally be in communication with the main reservoir to receive gas therefrom, and during actuation of the dispenser the liquid metering chamber and the gas holding chamber pass through an intermediate state in which the liquid metering chamber is sealed from the external environment and from the main reservoir and the gas holding chamber is sealed from the main reservoir, and a final state in which the liquid metering chamber is open to the environment and the two chambers are in communication with each other but each sealed from the main reservoir.

The liquid metering chamber and the gas holding chamber may also be sealed from each other in the intermediate state. In this case, it is preferable that during the transition from the intermediate state to the final state the two chambers are placed in communication before the liquid metering chamber is opened to the environment.

The liquid metering chamber functions in a manner similar to the metering chamber in a prior art dispenser, and its volume determines the volume of liquid discharged from the dispenser at each actuation. The gas holding chamber provides a small charge of pressurised gas to drive the liquid in the liquid metering chamber so that pressurised dispensing of the liquid in the metering chamber occurs. In theory, this advantage could be obtained by providing means to connect the liquid metering dispenser to the pressurised gas propellant in the main reservoir, but in this case if the outlet valve was not closed promptly

following discharge of the liquid from the metering chamber there would be a tendency for a complete loss of pressurising propellant from the dispenser. Thus it will be appreciated that the seal required between the gas holding chamber and the main reservoir can be relatively poor, provided that it is sufficient to avoid a general loss of pressurising gas during a normal dispensing operation. The quality of the seal between the liquid metering chamber and the main reservoir is more important, since any tendency for liquid to leak in either direction between the liquid metering chamber and the reservoir during discharge will alter the volume of liquid dispensed.

Advantageously, the dispenser has a longitudinally extending actuator body, which includes a discharge passage through which the liquid metering chamber is connected to the external environment in the final state of actuation of the dispenser, and movement of the actuator body from its normal position through an intermediate position to a final position seals the chambers from the reservoir and connects them together so as to bring about the said intermediate state of the chambers in the intermediate position of the body and the final state of the chambers in the final position of the body. Advantageously, the actuator body is resiliently biased to its normal position and movable against the bias to its intermediate position and on to its final position. Thus, the actuator body is automatically returned to its normal position when it is released, sealing the liquid metering chamber from the external environment and connecting the chambers to the reservoir for refilling.

Preferably, the actuator body is moved inwardly into the

dispenser during an acutating stroke from its normal position via its intermediate position to its final position.

5 Preferably stop means are provided to limit the travel of the actuator body away from the intermediate position beyond the normal and final positions.

10 The liquid metering chamber and the gas holding chamber will normally be spaced from one another, in which case the actuator body conveniently contains a passageway within it, which opens into the two chambers connecting them together in the final position of the body.

15 Preferably, the metering chamber is at the bottom of the dispenser when the dispenser is in its position of use, so that in the normal state of the chambers liquid from the main reservoir tends to fill the metering chamber under the influence of gravity.

20 The liquid metering chamber and the gas holding chamber may be provided spaced apart within a central core of the dispenser, the portion of the central core between the two chambers being open to the reservoir and open to the liquid metering chamber in its normal state to allow liquid to flow into the chamber, and the portion of the central core on the side of the gas holding chamber remote from the liquid metering chamber also being open to the reservoir and being open to the gas holding chamber in its
25 normal state to allow gas to flow into the chamber.

Normally, the gas holding chamber will be arranged to be higher than the liquid metering chamber when the dispenser is in its position of use, so that in the normal state

each chamber is open to the portion of the central core above it.

5 If the gas holding chamber is positioned sufficiently high within the dispenser to be above the level of liquid in the reservoir when the dispenser is in its position of use, the gas holding chamber may be arranged to be in communication with the main reservoir at its lowest point when in the normal state, to permit the draining from the chamber of any liquid which might accidentally have
10 entered the reservoir while the dispenser was in some other position. This drainage connection is preferably additional to the connection provided for entry of gas into the gas holding chamber, and is also closed in the intermediate and final states of the chamber during
15 actuation of the dispenser. Preferably, during transition from the normal state to the intermediate state of the chamber, the drainage connection is closed before the gas holding chamber is sealed from the main reservoir.

20 According to a second aspect of the present invention there is provided a holder for a pressurised metering dispenser, comprising means to support a dispenser in its position of use and means to cause relative movement between the main body of a supported dispenser and an actuating member through an actuating stroke, the means
25 for causing relative movement being itself manually actuatable.

Preferably, the holder also comprises means responsive to actuation of the means to cause relative movement, which provides a signal when a predetermined number of
30 actuations of the means for causing relative movement has occurred since a dispenser supported in the holder was

placed in position. The further means may be a counter which provides a signal in the form of a count value in response to each actuation of the means for causing relative movement. Alternatively, the further means may provide a warning signal, as for example a light or a
5 buzzer, only when the predetermined number of actuations has been reached. In either case, the further means can be used to warn an operator that the contents of a dispenser supported in the holder have been almost
10 entirely discharged. Conveniently, means is provided for varying predetermined number so that the number of actuations which occur before the warning signal is given can be varied to accommodate dispensers capable of discharging different numbers of metered doses.

15 Preferably, the holder has mounting means by which it may be mounted on a support surface with a supported dispenser in its position of use. This enables the dispenser to be located more accurately and more steadily with respect to a dish or the like in to which a dose of liquid is to be
20 discharged than if the holder had to be supported by hand.

The means for causing relative movement between the main body of the dispenser and its actuating member may be powered, and comprise a solenoid or a motor etc. However,
25 it is preferred that the means for causing relative movement is mechanical and driven by the manual actuation. In a preferred embodiment, this means comprises a lever one end of which bears on the dispenser and the other end of which is a manually operable trigger.

30 A holder according to the present invention provides a means of mounting and operating a pressurised metering

dispenser in a laboratory separately from an analyser such as is disclosed in my earlier applications. Thus, dispensers might be used mounted in such holders during sample preparation and in the performance of tests and analyses which do not need to be carried out in analysis apparatus.

In accordance with another aspect of the invention, a modification may be incorporated in the discharge tube of a dispenser such as not exclusively of the type so far described, by which an accurate sample volume of a liquid to be analysed can be collected and subsequently dispensed, together with a metered dose of reagent.

The modification comprises a resiliently biased sleeve which downwardly surrounds the lower end of the dispenser nozzle and is prevented from passing beyond the end of the nozzle, and a nozzle extension of known internal volume, which extend from the sleeve beyond the dispenser nozzle but can be displaced upwardly relative to the nozzle end by an upwardly directed force on the lower end thereof. In use the lower end of the nozzle extension is pushed against the base of a dish or reservoir containing a sample liquid so that the sleeve is fully retracted and the dispenser is then allowed to rise thereby trapping a small quantity of the sample liquid in the nozzle extension. The liquid is held in place by surface tension and air pressure.

After removing the dispenser from the liquid, the retained sample can be ejected together with a quantity of reagent from the dispenser reservoir, by normal activation of the dispenser. Mixing of the sample and the reagent occurs during ejection.

Apart from the problems of reagent metering with currently available equipment, similar problems arise with the requirement to meter samples for analysis because the same equipment is used.

5 However, there is a more serious drawback in that sample carryover or contamination of a sample by a previous one can be caused by retention of sample on the walls of the pipette tip. This is overcome by scrapping the tip after
10 each sample, or by wiping or washing the outside of the tip between samples, but the latter technique still leaves sample inside the tip. The only other way to avoid
15 carryover is to draw up and discharge a quantity of cleaning fluid between samples, but this is time consuming in manual pipetting, or leads to increased complexity in automatic samples.

Embodiments of the present invention, are given by way of non-limitative example, will now be described with reference to the accompanying drawings, in which:

20 Figure 1. is a partial sectional view of a pressurised metering dispenser embodying the present invention, in its normal state;

Figure 2. is a partial sectional view of the dispenser of Figure 1 in its final state of actuation;

25 Figure 3. is an overall view of the dispenser of Figures 1 and 2;

Figure 4. is a partial sectional view of a further dispenser embodying the present invention;

Figure 5. is a side view of a holder embodying the present invention;

Figure 6. is an end view of the holder of Figure 5,

Figure 7 is a cross-section through a discharge tube which incorporates a modification by which accurate sample volumes of a liquid to be analysed can be collected, and,

Figure 8 illustrates such a modified discharge tube placed in a well containing a liquid a sample volume of which is required to be collected.

10 Detailed description of the illustrated embodiments

Figures 1 to 3 illustrate a pressurised metering dispenser. The metering and dispensing mechanism is shown in section in Figures 1 and 2. In the dispenser, a main body 1 defines a main reservoir 3, which is charged with a volume of liquid 5 and pressurised gas 7. The gas 7 functions to drive liquid positively out of the dispenser during discharge, by virtue of its pressure. Accordingly, it is at a pressure above atmospheric, typically about 400 kPa gauge, or 500 kPa absolute. The gas is preferably selected to be insoluble and chemically unreactive with the liquid 5, and will commonly be nitrogen or argon.

A central core 9 runs within the main body 1 from its mouth sufficiently far for its end to be above the level of liquid in the reservoir 3 when the dispenser is held mouth downwardly. Preferably, it runs for substantially all of the length of the main body 1. Within the central core 9, seals 11, 13, 15, 17 define a liquid metering

chamber 19 and a gas holding chamber 21. In use, the volume of the liquid metering chamber 19 determines the volume of the metered dose of liquid dispensed from the dispenser in a single actuation.

5 An actuator body 23 is slidably mounted within the central core 9 and protrudes out through the mouth of the dispenser. It passes through the seals 11, 13, 15, 17 and co-operates with them to provide valves. Additionally, the actuator body 23 contains an internal gas passage 25
10 and an internal liquid discharge passage 27. Thus the actuator body 23 also functions as the discharge nozzle of the dispenser.

The actuator body 23 may conveniently be made of nylon or acetol; the valve seals may be made of nitrite butyl
15 rubber. However, it is possible that, for dispensing particularly aggressive liquids, it may be preferred to manufacture the body 23 of polypropylene or stainless steel and the seals of fluorocarbon rubber or PTFE based material.

20 A spring 29 acts on the actuator body 23 to bias it towards a normal position as shown in Figure 1. In this position, further movement of the actuator body 23 is prevented by a lower stop flange 31. In this position, the chambers 19, 21 are each in their normal states and
25 are in communication with the respective portions of the central core 9 above them.

The portion of the central core 9 between the liquid metering chamber 19 and the gas holding chamber 21 is in communication with the main reservoir 3 by means of
30 apertures 33. Accordingly, the portion of the central

core 9 immediately above the liquid metering chamber 19 is flooded with liquid 5, so that in the normal state of the liquid metering chamber as shown in Figure 1 it also is filled with liquid. The portion of the central core 9
5 above the gas holding chamber 21 is in communication with the main reservoir at its upper end, so that this portion of the central core 9 is filled with pressurised gas 7. Accordingly, in the normal state the gas holding chamber 21 fills with gas at the pressure prevailing within the
10 main reservoir 3.

In the normal state, both ends of the gas passage 25 are closed by seals 13, 17. The upper end of the liquid discharge passage 27 is also closed by seal 17 so that the inside of the dispenser is not in communication with the
15 external environment.

To actuate the dispenser, the actuator body 23 is pushed upwardly into the dispenser in the direction of arrow 35, against the action of the spring 29. Conveniently, the actuator body 23 may be moved by pressing against an
20 actuation flange 37.

As the actuator body moves upwardly out of its normal position, wider portions of it become level with the seals 11, 15 which define the upper ends of the chambers 19, 21. This closes the passageways through which these chambers
25 were in communication with the remaining portions of central core 9 and the main reservoir 3. The chambers 19, 21 thus enter a state in which they are sealed from each other and from the main reservoir 3.

As the actuator body 23 moves further up, the ends of the
30 gas passage 25 clear the seals 13, 17 and the liquid

metering chamber 19 and the gas holding chamber 21 are placed in communication with each other. The upper end of the liquid discharge passage 27 remains closed by the lowermost seal 17.

5 At the end of the actuation stroke, the actuator body 23 reaches its final position, shown in Figure 2, in which the upper end of the liquid discharge passage 27 clears the seal 17 and enters the liquid metering chamber 19. Since the liquid in the liquid metering chamber 19 is at
10 greater than atmospheric pressure, it begins to flow out of the dispenser through the discharge passage 27. As the liquid flows out of the metering chamber 19, the small charge of gas in the gas holding chamber 21 expands and passes through the gas passage 25 into the metering
15 chamber 19, and thus pressure continues to be applied to the liquid remaining in the metering chamber 19. In this manner, the gas from the gas holding chamber 21 drives all of the liquid in the liquid metering chamber 19 positively out through the discharge passage 27, ensuring that the
20 full metered dose of liquid is dispensed. Finally, the gas is vented to the atmosphere through the discharge passage 27, clearing any remaining liquid out of the passage and removing any droplets which may have formed at the nozzle of the dispenser.

25 The actuator body 23 is prevented from moving upwardly beyond its final actuation position by an upper stop flange 39.

On release of the external force applied to the actuation flange 37, the actuator body 23 moves downwardly under the
30 influence of the spring 29 to return to its normal position as shown in Figure 1, and the chambers 19, 21

refill with liquid 5 and gas 7 respectively from the main reservoir 3.

For ease of manufacturing, the actuator body 23 may be made in two separate pieces as is shown in Figures 1 and 2. Since the spring 29 acts on the upper piece of the actuator body 23, the two pieces are always pressed together in all positions of the actuator body 23.

The dispenser may also be provided with a snap-off security nozzle cover 40, as shown in broken lines in Figure 3.

Although the pressurised metering dispenser of Figures 1 to 3 is intended primarily to dispense a metered dose of liquid as a stream, a suitable known device may be fitted to the discharge nozzle end of the actuator body 23 to divide the discharge liquid into a spray or aerosol of finely divided droplets. Accordingly, the dispenser may be used for the same purposes as conventional metering dispensers using fluorocarbon propellents. This may be desirable from the environmental point of view, as it enables the fluorocarbons to be replaced by less harmful propellents.

Figure 4 shows an alternative dispenser embodying the present invention, in which the gas holding chamber 21 is positioned differently from the arrangement shown in Figures 1 and 2. In most respects, the dispenser of Figure 4 is the same as the dispenser of Figures 1 to 3, and like parts are given the same reference numerals. Although not shown in Figure 4, resilient means such as the spring 29 is provided to urge the actuator body 23 downwardly into the normal position, which is illustrated

in Figure 4.

In the embodiment of Figure 4, the gas holding chamber 21 is positioned at the end of the dispenser remote from the discharge nozzle and the liquid metering chamber 19.

5 Accordingly, the actuator body 23 has to extend for most of the length of the dispenser. In order to ensure that it remains correctly positioned, an apertured spacer ring 41 is provided within the central core 9, intermediate the liquid metering chamber 19 and the gas holding chamber 21.
10 The spacer ring 41 is apertured so that it has no sealing effect and does not tend to support liquid in the core 9 above it or alter the pressure on the liquid in the central core 9 below it.

When positioned as shown in Figure 4, the gas holding
15 chamber 21 is above the surface of the liquid 5 when the dispenser is in its position of use. This avoids any tendency for liquid 5 to flow into the chamber 21.

Additionally, in the normal state the gas holding chamber 21 in Figure 4 is open both at its top and at its bottom,
20 and the seal 13 is so shaped that the bottom surface of the gas holding chamber 21 slopes downwardly towards the lower opening. Accordingly, if any liquid 5 should enter the gas holding chamber 21, as may occur if the dispenser is inverted or laid on its side, the liquid will
25 immediately drain out of the chamber 21 through the lower opening when the dispenser is moved to its position of use. In this way, it is ensured that the gas holding chamber 21 is always filled with pressurised gas 7 and never contains any liquid 5 when the dispenser is actuated
30 in the correct manner, thus ensuring that the amount of liquid dispensed is correct and that there is sufficient gas in the gas holding chamber 21 to expel it

effectively.

As the actuator body 23 is moved upwardly into the dispenser during an actuating stroke, the lower opening of the gas holding chamber 21 is closed first, and then the upper opening is also closed, sealing the gas holding chamber 21 from the main reservoir 3. As in the embodiment of the Figures 1 to 3, after the two chambers 19, 21 have been sealed from the main reservoir 3, the ends of the gas passage 25 clear the seals 13, 17 and the chambers are placed in communication. Finally, the upper end of the liquid discharge passage 27 clears the lowermost seal 17 and the liquid in the liquid metering chamber 19 is discharged.

In contrast to the arrangement shown in Figure 3, the central core 9 in the embodiment of Figure 4 extends over the entire length of the dispenser, contacting the end surface of the main body 1 remote from the discharge nozzle, but has apertures 43 around its upper end. This feature may be combined with the mechanism shown in Figures 1 and 2, and the arrangement of the central core 9 shown in Figure 3 may be used with the mechanism shown in Figure 4.

The mechanism shown in Figure 4 may be varied by removing the opening at the top of the gas holding chamber 21 so that in its normal state the chamber 21 is only open downwardly. In this case, apertures would have to be provided in the central core 9 below the level of the gas holding chamber 21 so that in its normal state the chamber is in communication with the main reservoir 3. However, the arrangement shown in Figure 4 is preferred to this alternative since the upper opening from the gas holding

chamber 21 not only serves to place the chamber in communication with the main reservoir but acts as a gas inlet during draining of any liquid which might have entered the gas holding chamber 21. In the absence of such an upper opening liquid might fail to drain quickly and completely from the chamber when the dispenser is moved into its position of use.

The main body 1 of the dispenser will normally be metal, but other materials such as glass may be used provided that they can withstand the pressure within the dispenser. If the main body 1 is transparent an operator can see easily how much liquid 5 remains within the dispenser to be dispensed. However, it will often be preferred to make the main body 1 opaque in order to avoid photochemical effects on the liquid 5 from outside light.

The liquid 5 is prepared and introduced into the dispenser during manufacture under controlled conditions, so that it is relatively easy to guarantee that its formulation is correct. Because nothing enters the dispenser in use, the liquid is protected from oxidation, contamination etc, and its sterility is maintained.

Each successive dose is dispensed via the same liquid metering chamber 19, so that the repeatability of the doses (lack of variation in volume from dose to dose) is good.

Figures 5 and 6 show a holder 45 for a pressurised metering dispenser as shown in Figures 1 to 4. A dispenser 47 can be removably located in support means in a supporting arm 49, which holds the dispenser in its position of use with the tip of its discharge nozzle

raised slightly above the surface 51 of the bench on which the holder sits. Thus a sample-holding container may be placed under the nozzle of the dispenser 47 and a metered dose of the liquid in the dispenser may be discharged into the container as part of a sample preparation or analysis procedure.

The dispenser 47 is actuated by its main body being driven downwardly by one end of an actuating lever 53. The actuating lever 53 is pivoted part way along its length at 55, and its end remote from the dispenser 47 forms a manually operable trigger 57. Thus, an operator may grasp the upright portion 59 by hand from the rear with a finger on the trigger 57, and may apply a precisely metered dose of liquid from the dispenser 47 by squeezing the trigger 57 firmly. The holder 45 remains stably supported on the surface 51 of the bench or the like by its broad base portion 61.

At the top rear of the holder 45 there is a counter 63, with its display 65 visible to the operator. Operation of the trigger 57 to actuate the dispenser 47 will also depress a button 67 which operates the counter 63.

If the counter 63 is reset to zero when a fresh dispenser 47 is fitted into the holder 45, the counter display 65 can be arranged to display the number of actuations of the dispenser and thus the number of metered doses of liquid discharged from it. This provides the operator with a warning when the total number of metered doses available from the dispenser 47 is being approached. Alternatively, the counter 63 may be arranged to be set to the total number of doses within the dispenser 47 when the new dispenser is fitted and arranged to count down so that the

display 65 shows how many doses remain within the dispenser 47 to be discharged.

5 In addition to warning the operator that a dispenser 47 is nearly empty by means of the count on the counter display 65, the counter 63 may also give some other predetermined warning signal at a specific count, such as lighting a light, sounding an alarm or moving a shutter into or out of the area of the display 65 to present a warning mark to the operator.

10 The counter 63 may be electronic and powered by a small battery. Alternatively, it may be entirely mechanical and driven by the movement of the operating button 67.

15 Preferably, if the counter counts down from the total number of doses in the dispenser the initial count to which it is set can be varied. If a further signal is given that the dispenser 47 is nearly empty, in addition to the count value, then preferably the number of times the trigger 57 is operated before the further signal is given can be varied. In this way, the operation of the
20 counter 63 may be adapted to different dispensers 47 containing different numbers of doses.

25 It is also possible for attaching an atomiser or rebulizer to the dispenser, so that the dispensed liquid is dispersed into droplets in like manner to an aerosol spray.

Figure 7 shows a section through a modified discharge tube.

The tip 69 is lowered into contact with the bottom of the

liquid container, and by pressing down on the dispenser, the tube 71, slides through the tip 69 until it also touches the container bottom. When the dispenser is withdrawn, the sleeve 73 under the action of the spring 75 loaded sleeve 73 urges the tip 69 downwards and thus traps
5 a volume of liquid in chamber 77. The liquid is retained in the chamber by air pressure and surface tension, in known manner.

The dispenser is then held over a suitable receptacle and
10 operated as described hereinbefore which causes a metered volume of the dispenser contents to travel through the conduit 79, mix with and discharge the trapped sample in the chamber 77.

For convenience, the tip 69 and sleeve 73 may be
15 manufactured from a resilient plastics material. The tip 69 is removable by giving a firm pull, but is normally retained on tube 73 by a shoulder at 83 which also acts as a seal to prevent or reduce the ingress of air which would cause loss of sample. The shoulder 83 on the tip 69 is
20 also a slidable interface fit on tube 71 so that a depression is maintained inside tip 69 during sampling. The slots 81 in the tip 69 prevent blockage if the tip 69 is placed squarely on the liquid container bottom. The spring 75 is substantially weaker than the spring in the
25 dispenser so that there is less likelihood of discharging the dispenser contents into the sample container during sampling.

As a result of the modifications the dispenser possesses the following advantages:-

- 30 1. The inside of the tip 69 is washed by the metered volume of reagent from the dispenser, and it is necessary

only to wipe the outside of the tip to ensure zero carryover.

2. The sample volume may be varied easily by fitting a tip of different length.

5 3. A complete cycle of sampling and adding reagent is accomplished in less than half the time required when using existing methods.

4. There is a good mixing of the two liquids during dispensing.

10 5. Because there is an excess of metered gas during each operation of the dispenser, the complete conduit and tip is emptied each time.

6. Manual or automatic equipment would use exactly the same sampler/dispenser.

15 7. Solid displacement pipetting.

As will be apparent to those skilled in the art, many variations on the illustrated embodiments are possible.

CLAIMS

1. A pressurised metering dispenser comprising a main reservoir, a liquid metering chamber and a gas holding chamber, arranged so that if the main reservoir is charged with a liquid and a pressurising gas and the dispenser is held in its position of use, the liquid metering chamber will normally be sealed from the environment and be in communication with the main reservoir to receive liquid therefrom and the gas holding chamber will normally be in communication with the main reservoir to receive gas therefrom, and during actuation of the dispenser the liquid metering chamber and the gas holding chamber pass through an intermediate state in which the liquid metering chamber is sealed from the external environment and from the main reservoir and the gas holding chamber is sealed from the main reservoir, and a final state in which the liquid metering chamber is open to the environment and the two chambers are in communication with each other but each sealed from the main reservoir.
2. A pressurised metering dispenser as claimed in claim 1 in which the liquid metering chamber and the gas holding chamber are also sealed from each other in the intermediate state.
3. A pressurised metering dispenser as claimed in claim 2

in which during the transition from the intermediate state to the final state the two chambers are placed in communication before the liquid metering chamber is opened to the environment.

5 4. A pressurised metering dispenser as claimed in any of
claims 1 to 3 in which the dispenser has a longitudinally
extending actuator body, which includes a discharge
passage through which the liquid metering chamber is
connected to the external environment in the final state
10 of actuation of the dispenser, and movement of the
actuator body from its normal position through an
intermediate position to a final position seals the
chambers from the reservoir and connects them together so
as to bring about the said intermediate state of the
15 chambers in the intermediate position of the body and the
final state of the chambers in the final position of the
body.

5. A pressurised metering dispenser as claimed in claim 4
wherein the actuator body is resiliently biased to its
20 normal position and movable against the bias to its
intermediate position and on to its final position,
whereby the actuator body is automatically returned to its
normal position when it is released, sealing the liquid
metering chamber from the external environment and
25 connecting the chambers to the reservoir for refilling.

6. A pressurised metering dispenser as claimed in any of
the preceding claims in which the actuator body is moved
inwardly into the dispenser during an actuating stroke
from its normal position via its intermediate position to
30 its final position.

7. A pressurised metering dispenser as claimed in claim 6 in which stop means are provided to limit the travel of the actuator body away from the intermediate position beyond the normal and final positions.

5 8. A pressurised metering dispenser in any of the preceding claims in which the liquid metering chamber and the gas holding chamber are spaced from one another and the actuator body contains a passageway within it, which opens into the two chambers connecting them together in
10 the final position of the body.

9. A pressurised metering dispenser as claimed in any of the preceding claims in which the metering chamber is at the bottom of the dispenser when the dispenser is in its position of use, so that in the normal state of the
15 chambers liquid from the main reservoir tends to fill the metering chamber under the influence of gravity.

10. A pressurised metering dispenser as claimed in any of the preceding claims, in which the liquid metering chamber and the gas holding chamber are provided spaced apart
20 within a central core of the dispenser, the portion of the central core between the two chambers being open to the reservoir and open to the liquid metering chamber in its normal state to allow liquid to flow into the chamber, and the portion of the central core on the side of the gas
25 holding chamber remote from the liquid metering chamber is also open to the reservoir and is open to the gas holding chamber in its normal state to allow gas to flow into the chamber.

11. A pressurised metering dispenser in any of the
30 preceding claims in which the gas holding chamber is

arranged to be higher than the liquid metering chamber when the dispenser is in its position of use, so that in the normal state each chamber is open to the portion of the central core above it.

5 12. A pressurised metering dispenser as claimed in any of
the preceding claims in which the gas holding chamber is
positioned sufficiently high within the dispenser to be
above the level of the liquid in the reservoir when the
dispenser is in its position of use so that the gas
10 holding chamber can communicate with the main reservoir at
its lowest point when in the normal state, to permit the
draining from the chamber of any liquid which might
accidentally have entered the reservoir while the
dispenser was in some other position.

15 13. A pressurised metering dispenser as claimed in claim
12 wherein the drainage connection is additional to the
connection provided for entry of gas into the gas holding
chamber, and is also closed in the intermediate and final
states of the chamber during actuation of the dispenser.

20 14. A pressurised metering dispenser as claimed in claim
12 or 13 wherein, during transition from the normal state
to the intermediate state of the chamber, the drainage
connection is closed before the gas holding chamber is
sealed from the main reservoir.

25 15. A holder for a pressurised metering dispenser,
comprising means to support a dispenser in its position of
use and means to cause relative movement between the main
body of a supported dispenser and an actuating member
through an actuating stroke, the means for causing
30 relative movement being itself manually actuable.

16. A holder as claimed in claim 15 which also comprises means responsive to actuation of the means to cause relative movement, which provides a signal when a predetermined number of actuations of the means for causing relative movement has occurred since a dispenser was last placed in position.

17. A holder as claimed in claim 16 wherein the further means comprises a counter which provides a signal in the form of a count value in response to each actuation of the means for causing relative movement.

18. A holder as claimed in claim 16 wherein the further means provides a warning signal, as for example a light or a buzzer, only when a predetermined number of actuations has been reached.

19. A holder as claimed in any of claims 16 to 18 wherein means is provided for varying the predetermined number so that the number of actuations which occur before the warning signal is given can be varied to accommodate dispensers capable of discharging different numbers of metered doses.

20. A holder as claimed in any of claims 16 to 19 wherein the holder has mounting means by which it is mountable on a support surface with a supported dispenser in its position of use, so as to enable the dispenser to be located accurately and steadily with respect to a dish or the like into which a dose of liquid is to be discharged.

21. A holder as claimed in any of claims 16 to 20 wherein the means for causing relative movement between the main

body of the dispenser and its actuating member is powered such as by a solenoid or a motor.

22. A holder as claimed in any of claims 16 to 21 wherein the means for causing relative movement is mechanical and is driven by the manual actuation.

23. A holder as claimed in claim 22 wherein the mechanical means comprises a lever one end of which bears on the dispenser and the other end of which is a manually operable trigger.

24. A dispenser for collecting a sample volume of a liquid to be analysed for subsequent dispensing with a reagent wherein the dispenser includes a nozzle through which reagent can be ejected in manner known per se, and at least the lower end of the nozzle is surrounded by a sleeve which is resiliently displaceable in one direction to expose the lower end of the nozzle, the lower end of the sleeve defining a volume into which a liquid can be drawn by movement of the lower nozzle end in an upward direction relative to the lower end of the sleeve.

25. A dispenser as described in any of claims 1 to 14 which includes a nozzle through which reagent is ejected during dispensing and which further includes a sleeve around at least the lower end of the nozzle which is resiliently displaceable in a direction to expose the lower end of the nozzle, the lower end of the sleeve defining a volume into which a liquid can be drawn by movement of the lower nozzle end in an upward direction relative to the lower end of the sleeve.

26. A pressurised metering dispenser constructed arranged

and adapted to operate substantially as herein described with reference to and as illustrated in Figure 1, or Figure 2 or Figure 3 or Figure 4 of the accompanying drawings.

5 27. A holder for a dispenser constructed arranged and adapted to operate substantially as herein described with reference to and as illustrated in Figure 5 and Figure 6 of the accompanying drawings.

10 28. A dispenser constructed arranged and adapted to operate substantially as herein described with reference to and as illustrated in Figure 6 and Figure 7 of the accompanying drawings.

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